

MAR 17 2001

SEQUENCE LISTING

<110> Nicolaides, Nicholas C  
Grasso, Luigi  
Sass, Philip M

<120> METHODS FOR GENERATING GENETICALLY ALTERED  
ANTIBODY-PRODUCING CELL LINES WITH IMPROVED ANTIBODY  
CHARACTERISTICS

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<140> 09/707,468

<141> 2000-11-07

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<170> PatentIn Ver. 2.1

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<213> Artificial Sequence

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<211> 859

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Ala Gly Ala Thr Thr Ile Asp Leu Arg Leu Lys Asp Tyr Gly Val Asp		
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Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe		
65	70	75
80		
Glu Gly Leu Ala Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala		
85	90	95
Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser		
100	105	110
Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Gly Ser		
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Ala Ser Val Gly Thr Arg Leu Val Phe Asp His Asn Gly Lys Ile Thr		
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Gln Lys Thr Pro Tyr Pro Arg Pro Lys Gly Thr Thr Val Ser Val Gln		
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His Leu Phe Tyr Thr Leu Pro Val Arg Tyr Lys Glu Phe Gln Arg Asn		
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Ile Lys Lys Glu Tyr Ser Lys Met Val Gln Val Leu Gln Ala Tyr Cys		
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Ile Ile Ser Ala Gly Val Arg Val Ser Cys Thr Asn Gln Leu Gly Gln		
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Gly Lys Arg His Ala Val Val Cys Thr Ser Gly Thr Ser Gly Met Lys		
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Glu Asn Ile Gly Ser Val Phe Gly Gln Lys Gln Leu Gln Ser Leu Ile		
225	230	235
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Pro Phe Val Gln Leu Pro Pro Ser Asp Ala Val Cys Glu Glu Tyr Gly		
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Ser Glu Lys Arg Gly Val Leu Ser Ser Tyr Pro Ser Asp Val Ile Ser				
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Leu Ser Ser Thr Ser Ala Gly Ser Glu Glu Glu Phe Ser Thr Pro Glu				
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Val Ala Ser Ser Phe Ser Ser Asp Tyr Asn Val Ser Ser Leu Glu Asp				
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Arg Pro Ser Gln Glu Thr Ile Asn Cys Gly Asp Leu Asp Cys Arg Pro				

530

535

540

Pro Gly Thr Gly Gln Ser Leu Lys Pro Glu Asp His Gly Tyr Gln Cys  
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Lys Ala Leu Pro Leu Ala Arg Leu Ser Pro Thr Asn Ala Lys Arg Phe  
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Lys Thr Glu Glu Arg Pro Ser Asn Val Asn Ile Ser Gln Arg Leu Pro  
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Gly Pro Gln Ser Thr Ser Ala Ala Glu Val Asp Val Ala Ile Lys Met  
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Asn Lys Arg Ile Val Leu Leu Glu Phe Ser Leu Ser Ser Leu Ala Lys  
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Arg Met Lys Gln Leu Gln His Leu Lys Ala Gln Asn Lys His Glu Leu  
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Ser Tyr Arg Lys Phe Arg Ala Lys Ile Cys Pro Gly Glu Asn Gln Ala  
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Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Ser Met Phe Ala Glu  
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Met Glu Ile Leu Gly Gln Phe Asn Leu Gly Phe Ile Val Thr Lys Leu  
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Lys Glu Asp Leu Phe Leu Val Asp Gln His Ala Ala Asp Glu Lys Tyr  
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Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Ala Gln Arg Leu  
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Ile Thr Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu Ala Val Leu  
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Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp Phe Val Ile  
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Asp Glu Asp Ala Pro Val Thr Glu Arg Ala Lys Leu Ile Ser Leu Pro  
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Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Ile Asp Glu Leu Ile  
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Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro Ser Arg Val

785

790

795

800

Arg Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val Met Ile Gly  
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Thr Ala Leu Asn Ala Ser Glu Met Lys Lys Leu Ile Thr His Met Gly  
820 825 830

Glu Met Asp His Pro Trp Asn Cys Pro His Gly Arg Pro Thr Met Arg  
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His Val Ala Asn Leu Asp Val Ile Ser Gln Asn  
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&lt;210&gt; 6

&lt;211&gt; 3056

&lt;212&gt; DNA

&lt;213&gt; Mus musculus

&lt;400&gt; 6

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<213> Homo sapiens

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20

25

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Leu Ser Leu Ser Thr Ala Val Lys Glu Leu Val Glu Asn Ser Leu Asp

35

40

45

Ala Gly Ala Thr Asn Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp

50

55

60

Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe

65

70

75

80

Glu Gly Leu Thr Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala

Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser  
100 105 110

Ser Leu Cys Ala Leu Ser Asp Val Thr Ile Ser Thr Cys His Ala Ser  
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Ala Lys Val Gly Thr Arg Leu Met Phe Asp His Asn Gly Lys Ile Ile  
130 135 140

Gln Lys Thr Pro Tyr Pro Arg Pro Arg Gly Thr Thr Val Ser Val Gln  
145 150 155 160

Gln Leu Phe Ser Thr Leu Pro Val Arg His Lys Glu Phe Gln Arg Asn  
165 170 175

Ile Lys Lys Glu Tyr Ala Lys Met Val Gln Val Leu His Ala Tyr Cys  
180 185 190

Ile Ile Ser Ala Gly Ile Arg Val Ser Cys Thr Asn Gln Leu Gly Gln  
195 200 205

Gly Lys Arg Gln Pro Val Val Cys Thr Gly Gly Ser Pro Ser Ile Lys  
210 215 220

Glu Asn Ile Gly Ser Val Phe Gly Gln Lys Gln Leu Gln Ser Leu Ile  
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Pro Phe Val Gln Leu Pro Pro Ser Asp Ser Val Cys Glu Glu Tyr Gly  
245 250 255

Leu Ser Cys Ser Asp Ala Leu His Asn Leu Phe Tyr Ile Ser Gly Phe  
260 265 270

Ile Ser Gln Cys Thr His Gly Val Gly Arg Ser Ser Thr Asp Arg Gln  
275 280 285

Phe Phe Phe Ile Asn Arg Arg Pro Cys Asp Pro Ala Lys Val Cys Arg  
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Leu Val Asn Glu Val Tyr His Met Tyr Asn Arg His Gln Tyr Pro Phe  
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Val Val Leu Asn Ile Ser Val Asp Ser Glu Cys Val Asp Ile Asn Val  
325 330 335

Thr Pro Asp Lys Arg Gln Ile Leu Leu Gln Glu Glu Lys Leu Leu Leu



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Lys Leu Asn Val Ser Gln Gln Pro Leu Leu Asp Val Glu Gly Asn Leu		
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Ile Lys Met His Ala Ala Asp Leu Glu Lys Pro Met Val Glu Lys Gln		
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Asp Gln Ser Pro Ser Leu Arg Thr Gly Glu Glu Lys Lys Asp Val Ser		
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Lys Pro His Ser Pro Lys Thr Pro Glu Pro Arg Arg Ser Pro Leu Gly		
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Gln Lys Arg Gly Met Leu Ser Ser Ser Thr Ser Gly Ala Ile Ser Asp		
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Lys Gly Val Leu Arg Pro Gln Lys Glu Ala Val Ser Ser Ser His Gly		
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Ser Gln Glu His Val Asp Ser Gln Glu Lys Ala Pro Glu Thr Asp Asp		
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Lys Phe Arg Val Leu Pro Gln Pro Thr Asn Leu Ala Thr Pro Asn Thr		
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Lys Leu Val Asn Thr Gln Asp Met Ser Ala Ser Gln Val Asp Val Ala		

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605

Val Lys Ile Asn Lys Lys Val Val Pro Leu Asp Phe Ser Met Ser Ser  
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Leu Ala Lys Arg Ile Lys Gln Leu His His Glu Ala Gln Gln Ser Glu  
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Gly Glu Gln Asn Tyr Arg Lys Phe Arg Ala Lys Ile Cys Pro Gly Glu  
645 650 655

Asn Gln Ala Ala Glu Asp Glu Leu Arg Lys Glu Ile Ser Lys Thr Met  
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Phe Ala Glu Met Glu Ile Ile Gly Gln Phe Asn Leu Gly Phe Ile Ile  
675 680 685

Thr Lys Leu Asn Glu Asp Ile Phe Ile Val Asp Gln His Ala Thr Asp  
690 695 700

Glu Lys Tyr Asn Phe Glu Met Leu Gln Gln His Thr Val Leu Gln Gly  
705 710 715 720

Gln Arg Leu Ile Ala Pro Gln Thr Leu Asn Leu Thr Ala Val Asn Glu  
725 730 735

Ala Val Leu Ile Glu Asn Leu Glu Ile Phe Arg Lys Asn Gly Phe Asp  
740 745 750

Phe Val Ile Asp Glu Asn Ala Pro Val Thr Glu Arg Ala Lys Leu Ile  
755 760 765

Ser Leu Pro Thr Ser Lys Asn Trp Thr Phe Gly Pro Gln Asp Val Asp  
770 775 780

Glu Leu Ile Phe Met Leu Ser Asp Ser Pro Gly Val Met Cys Arg Pro  
785 790 795 800

Ser Arg Val Lys Gln Met Phe Ala Ser Arg Ala Cys Arg Lys Ser Val  
805 810 815

Met Ile Gly Thr Ala Leu Asn Thr Ser Glu Met Lys Lys Leu Ile Thr  
820 825 830

His Met Gly Glu Met Asp His Pro Trp Asn Cys Pro His Gly Arg Pro  
835 840 845

Thr Met Arg His Ile Ala Asn Leu Gly Val Ile Ser Gln Asn

&lt;210&gt; 8

&lt;211&gt; 2771

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 8

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<213> Homo sapiens

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Phe Asp Lys Ile Glu Val Arg Asp Asn Gly Glu Gly Ile Lys Ala Val  
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Asp Ala Pro Val Met Ala Met Lys Tyr Tyr Thr Ser Lys Ile Asn Ser  
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His Glu Asp Leu Glu Asn Leu Thr Thr Tyr Gly Phe Arg Gly Glu Ala  
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Leu Gly Ser Ile Cys Cys Ile Ala Glu Val Leu Ile Thr Thr Arg Thr  
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Ala Ala Asp Asn Phe Ser Thr Gln Tyr Val Leu Asp Gly Ser Gly His  
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Thr Ala Lys Lys Cys Lys Asp Glu Ile Lys Lys Ile Gln Asp Leu Leu  
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Phe	Gln	Tyr	His	Ser	Glu	Glu	Ser	Gln	Ile	Tyr	Leu	Ser	Gly	Phe	Leu	225	230	235
Pro	Lys	Cys	Asp	Ala	Asp	His	Ser	Phe	Thr	Ser	Leu	Ser	Thr	Pro	Glu	245	250	255
Arg	Ser	Phe	Ile	Phe	Ile	Asn	Ser	Arg	Pro	Val	His	Gln	Lys	Asp	Ile	260	265	270
Leu	Lys	Leu	Ile	Arg	His	His	Tyr	Asn	Leu	Lys	Cys	Leu	Lys	Glu	Ser	275	280	285
Thr	Arg	Leu	Tyr	Pro	Val	Phe	Phe	Leu	Lys	Ile	Asp	Val	Pro	Thr	Ala	290	295	300
Asp	Val	Asp	Val	Asn	Leu	Thr	Pro	Asp	Lys	Ser	Gln	Val	Leu	Leu	Gln	305	310	315
Asn	Lys	Glu	Ser	Val	Leu	Ile	Ala	Leu	Glu	Asn	Leu	Met	Thr	Thr	Cys	325	330	335
Tyr	Gly	Pro	Leu	Pro	Ser	Thr	Asn	Ser	Tyr	Glu	Asn	Asn	Lys	Thr	Asp	340	345	350
Val	Ser	Ala	Ala	Asp	Ile	Val	Leu	Ser	Lys	Thr	Ala	Glu	Thr	Asp	Val	355	360	365
Leu	Phe	Asn	Lys	Val	Glu	Ser	Ser	Gly	Lys	Asn	Tyr	Ser	Asn	Val	Asp	370	375	380
Thr	Ser	Val	Ile	Pro	Phe	Gln	Asn	Asp	Met	His	Asn	Asp	Glu	Ser	Gly	385	390	395
Lys	Asn	Thr	Asp	Asp	Cys	Leu	Asn	His	Gln	Ile	Ser	Ile	Gly	Asp	Phe	405	410	415
Gly	Tyr	Gly	His	Cys	Ser	Ser	Glu	Ile	Ser	Asn	Ile	Asp	Lys	Asn	Thr	420	425	430

Lys Asn Ala Phe Gln Asp Ile Ser Met Ser Asn Val Ser Trp Glu Asn  
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 Glu Trp Ser Arg Gly Asn Ile Leu Lys Asn Ser Val Gly Glu Asn Ile  
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 Glu Pro Val Lys Ile Leu Val Pro Glu Lys Ser Leu Pro Cys Lys Val  
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 675 680 685

Arg Arg Ser Gln Asn Ile Lys Met Val Gln Ile Pro Phe Ser Met Lys  
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 785 790 795 800  
 Arg Tyr Ser Gly Ser Thr Tyr Leu Ser Asp Pro Arg Leu Thr Ala Asn  
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 Gly Phe Lys Ile Lys Leu Ile Pro Gly Val Ser Ile Thr Glu Asn Tyr  
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 Leu Glu Ile Glu Gly Met Ala Asn Cys Leu Pro Phe Tyr Gly Val Ala  
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 Asp Leu Lys Glu Ile Leu Asn Ala Ile Leu Asn Arg Asn Ala Lys Glu  
 850 855 860  
 Val Tyr Glu Cys Arg Pro Arg Lys Val Ile Ser Tyr Leu Glu Gly Glu  
 865 870 875 880  
 Ala Val Arg Leu Ser Arg Gln Leu Pro Met Tyr Leu Ser Lys Glu Asp  
 885 890 895  
 Ile Gln Asp Ile Ile Tyr Arg Met Lys His Gln Phe Gly Asn Glu Ile  
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 Lys Glu Cys Val His Gly Arg Pro Phe Phe His His Leu Thr Tyr Leu  
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 Pro Glu Thr Thr  
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 gttctcagat catcacttcg gtggtcagtg ttgtaaaaga gcttattgaa aactccttgg 180  
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 aagccctgct atttaaaaga cttcttgaga atcataaact tctgcagag ccactggaaa 2400



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3063

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<210> 11

<211> 934

<212> PRT

<213> Homo sapiens

<400> 11

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Val Gly Phe Val Arg Phe Phe Gln Gly Met Pro Glu Lys Pro Thr Thr
          20                      25                      30

```

```

Thr Val Arg Leu Phe Asp Arg Gly Asp Phe Tyr Thr Ala His Gly Glu
          35                      40                      45

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```

Asp Ala Leu Leu Ala Ala Arg Glu Val Phe Lys Thr Gln Gly Val Ile
          50                      55                      60

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Lys Tyr Met Gly Pro Ala Gly Ala Lys Asn Leu Gln Ser Val Val Leu
          65                      70                      75                      80

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```

Ser Lys Met Asn Phe Glu Ser Phe Val Lys Asp Leu Leu Leu Val Arg
          85                      90                      95

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Gln Tyr Arg Val Glu Val Tyr Lys Asn Arg Ala Gly Asn Lys Ala Ser
          100                      105                      110

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Lys Glu Asn Asp Trp Tyr Leu Ala Tyr Lys Ala Ser Pro Gly Asn Leu
          115                      120                      125

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Ser Gln Phe Glu Asp Ile Leu Phe Gly Asn Asn Asp Met Ser Ala Ser
          130                      135                      140

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Ile Gly Val Val Gly Val Lys Met Ser Ala Val Asp Gly Gln Arg Gln

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Glu Phe Pro Asp Asn Asp Gln Phe Ser Asn Leu Glu Ala Leu Leu Ile						
	180		185		190	
Gln Ile Gly Pro Lys Glu Cys Val Leu Pro Gly Gly Glu Thr Ala Gly						
	195		200		205	
Asp Met Gly Lys Leu Arg Gln Ile Ile Gln Arg Gly Gly Ile Leu Ile						
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Thr Glu Arg Lys Lys Ala Asp Phe Ser Thr Lys Asp Ile Tyr Gln Asp						
	225		230		235	240
Leu Asn Arg Leu Leu Lys Gly Lys Lys Gly Glu Gln Met Asn Ser Ala						
		245		250		255
Val Leu Pro Glu Met Glu Asn Gln Val Ala Val Ser Ser Leu Ser Ala						
	260		265		270	
Val Ile Lys Phe Leu Glu Leu Leu Ser Asp Asp Ser Asn Phe Gly Gln						
	275		280		285	
Phe Glu Leu Thr Thr Phe Asp Phe Ser Gln Tyr Met Lys Leu Asp Ile						
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Ala Ala Val Arg Ala Leu Asn Leu Phe Gln Gly Ser Val Glu Asp Thr						
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Thr Gly Ser Gln Ser Leu Ala Ala Leu Leu Asn Lys Cys Lys Thr Pro						
		325		330		335
Gln Gly Gln Arg Leu Val Asn Gln Trp Ile Lys Gln Pro Leu Met Asp						
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Lys Asn Arg Ile Glu Glu Arg Leu Asn Leu Val Glu Ala Phe Val Glu						
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Asp Ala Glu Leu Arg Gln Thr Leu Gln Glu Asp Leu Leu Arg Arg Phe						
	370		375		380	
Pro Asp Leu Asn Arg Leu Ala Lys Lys Phe Gln Arg Gln Ala Ala Asn						
	385		390		395	400
Leu Gln Asp Cys Tyr Arg Leu Tyr Gln Gly Ile Asn Gln Leu Pro Asn						

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Leu Ala Val Phe Val Thr Pro Leu Thr Asp Leu Arg Ser Asp Phe Ser		
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Lys Phe Gln Glu Met Ile Glu Thr Thr Leu Asp Met Asp Gln Val Glu		
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Asn His Glu Phe Leu Val Lys Pro Ser Phe Asp Pro Asn Leu Ser Glu		
465	470	475
Leu Arg Glu Ile Met Asn Asp Leu Glu Lys Lys Met Gln Ser Thr Leu		
485	490	495
Ile Ser Ala Ala Arg Asp Leu Gly Leu Asp Pro Gly Lys Gln Ile Lys		
500	505	510
Leu Asp Ser Ser Ala Gln Phe Gly Tyr Tyr Phe Arg Val Thr Cys Lys		
515	520	525
Glu Glu Lys Val Leu Arg Asn Asn Lys Asn Phe Ser Thr Val Asp Ile		
530	535	540
Gln Lys Asn Gly Val Lys Phe Thr Asn Ser Lys Leu Thr Ser Leu Asn		
545	550	555
Glu Glu Tyr Thr Lys Asn Lys Thr Glu Tyr Glu Glu Ala Gln Asp Ala		
565	570	575
Ile Val Lys Glu Ile Val Asn Ile Ser Ser Gly Tyr Val Glu Pro Met		
580	585	590
Gln Thr Leu Asn Asp Val Leu Ala Gln Leu Asp Ala Val Val Ser Phe		
595	600	605
Ala His Val Ser Asn Gly Ala Pro Val Pro Tyr Val Arg Pro Ala Ile		
610	615	620
Leu Glu Lys Gly Gln Gly Arg Ile Ile Leu Lys Ala Ser Arg His Ala		
625	630	635
Cys Val Glu Val Gln Asp Glu Ile Ala Phe Ile Pro Asn Asp Val Tyr		
645	650	655
Phe Glu Lys Asp Lys Gln Met Phe His Ile Ile Thr Gly Pro Asn Met		

660

665

670

Gly Gly Lys Ser Thr Tyr Ile Arg Gln Thr Gly Val Ile Val Leu Met  
675 680 685

Ala Gln Ile Gly Cys Phe Val Pro Cys Glu Ser Ala Glu Val Ser Ile  
690 695 700

Val Asp Cys Ile Leu Ala Arg Val Gly Ala Gly Asp Ser Gln Leu Lys  
705 710 715 720

Gly Val Ser Thr Phe Met Ala Glu Met Leu Glu Thr Ala Ser Ile Leu  
725 730 735

Arg Ser Ala Thr Lys Asp Ser Leu Ile Ile Ile Asp Glu Leu Gly Arg  
740 745 750

Gly Thr Ser Thr Tyr Asp Gly Phe Gly Leu Ala Trp Ala Ile Ser Glu  
755 760 765

Tyr Ile Ala Thr Lys Ile Gly Ala Phe Cys Met Phe Ala Thr His Phe  
770 775 780

His Glu Leu Thr Ala Leu Ala Asn Gln Ile Pro Thr Val Asn Asn Leu  
785 790 795 800

His Val Thr Ala Leu Thr Thr Glu Glu Thr Leu Thr Met Leu Tyr Gln  
805 810 815

Val Lys Lys Gly Val Cys Asp Gln Ser Phe Gly Ile His Val Ala Glu  
820 825 830

Leu Ala Asn Phe Pro Lys His Val Ile Glu Cys Ala Lys Gln Lys Ala  
835 840 845

Leu Glu Leu Glu Glu Phe Gln Tyr Ile Gly Glu Ser Gln Gly Tyr Asp  
850 855 860

Ile Met Glu Pro Ala Ala Lys Lys Cys Tyr Leu Glu Arg Glu Gln Gly  
865 870 875 880

Glu Lys Ile Ile Gln Glu Phe Leu Ser Lys Val Lys Gln Met Pro Phe  
885 890 895

Thr Glu Met Ser Glu Glu Asn Ile Thr Ile Lys Leu Lys Gln Leu Lys  
900 905 910

Ala Glu Val Ile Ala Lys Asn Asn Ser Phe Val Asn Glu Ile Ile Ser

Arg Ile Lys Val Thr Thr  
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<210> 12

<211> 3145

<212> DNA

<213> Homo sapiens

<400> 12

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<210> 13

<211> 756

<212> PRT

<213> Homo sapiens

<400> 13

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Lys Glu Met Ile Glu Asn Cys Leu Asp Ala Lys Ser Thr Ser Ile Gln
      35              40              45

Val Ile Val Lys Glu Gly Gly Leu Lys Leu Ile Gln Ile Gln Asp Asn
      50              55              60

Gly Thr Gly Ile Arg Lys Glu Asp Leu Asp Ile Val Cys Glu Arg Phe
      65              70              75              80

Thr Thr Ser Lys Leu Gln Ser Phe Glu Asp Leu Ala Ser Ile Ser Thr
      85              90              95

Tyr Gly Phe Arg Gly Glu Ala Leu Ala Ser Ile Ser His Val Ala His
      100              105              110

Val Thr Ile Thr Thr Lys Thr Ala Asp Gly Lys Cys Ala Tyr Arg Ala
      115              120              125

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Ser Tyr Ser Asp Gly Lys Leu Lys Ala Pro Pro Lys Pro Cys Ala Gly  
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Asn Gln Gly Thr Gln Ile Thr Val Glu Asp Leu Phe Tyr Asn Ile Ala  
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Thr Arg Arg Lys Ala Leu Lys Asn Pro Ser Glu Glu Tyr Gly Lys Ile  
 165 170 175

Leu Glu Val Val Gly Arg Tyr Ser Val His Asn Ala Gly Ile Ser Phe  
 180 185 190

Ser Val Lys Lys Gln Gly Glu Thr Val Ala Asp Val Arg Thr Leu Pro  
 195 200 205

Asn Ala Ser Thr Val Asp Asn Ile Arg Ser Ile Phe Gly Asn Ala Val  
 210 215 220

Ser Arg Glu Leu Ile Glu Ile Gly Cys Glu Asp Lys Thr Leu Ala Phe  
 225 230 235 240

Lys Met Asn Gly Tyr Ile Ser Asn Ala Asn Tyr Ser Val Lys Lys Cys  
 245 250 255

Ile Phe Leu Leu Phe Ile Asn His Arg Leu Val Glu Ser Thr Ser Leu  
 260 265 270

Arg Lys Ala Ile Glu Thr Val Tyr Ala Ala Tyr Leu Pro Lys Asn Thr  
 275 280 285

His Pro Phe Leu Tyr Leu Ser Leu Glu Ile Ser Pro Gln Asn Val Asp  
 290 295 300

Val Asn Val His Pro Thr Lys His Glu Val His Phe Leu His Glu Glu  
 305 310 315 320

Ser Ile Leu Glu Arg Val Gln Gln His Ile Glu Ser Lys Leu Leu Gly  
 325 330 335

Ser Asn Ser Ser Arg Met Tyr Phe Thr Gln Thr Leu Leu Pro Gly Leu  
 340 345 350

Ala Gly Pro Ser Gly Glu Met Val Lys Ser Thr Thr Ser Leu Thr Ser  
 355 360 365

Ser Ser Thr Ser Gly Ser Ser Asp Lys Val Tyr Ala His Gln Met Val  
 370 375 380

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	405	410	415
Thr Asp Ile Ser Ser Gly Arg Ala Arg Gln Gln Asp Glu Glu Met Leu			
	420	425	430
Glu Leu Pro Ala Pro Ala Glu Val Ala Ala Lys Asn Gln Ser Leu Glu			
	435	440	445
Gly Asp Thr Thr Lys Gly Thr Ser Glu Met Ser Glu Lys Arg Gly Pro			
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Thr Ser Ser Asn Pro Arg Lys Arg His Arg Glu Asp Ser Asp Val Glu			
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Met Val Glu Asp Asp Ser Arg Lys Glu Met Thr Ala Ala Cys Thr Pro			
	485	490	495
Arg Arg Arg Ile Ile Asn Leu Thr Ser Val Leu Ser Leu Gln Glu Glu			
	500	505	510
Ile Asn Glu Gln Gly His Glu Val Leu Arg Glu Met Leu His Asn His			
	515	520	525
Ser Phe Val Gly Cys Val Asn Pro Gln Trp Ala Leu Ala Gln His Gln			
	530	535	540
Thr Lys Leu Tyr Leu Leu Asn Thr Thr Lys Leu Ser Glu Glu Leu Phe			
	545	550	555
Tyr Gln Ile Leu Ile Tyr Asp Phe Ala Asn Phe Gly Val Leu Arg Leu			
	565	570	575
Ser Glu Pro Ala Pro Leu Phe Asp Leu Ala Met Leu Ala Leu Asp Ser			
	580	585	590
Pro Glu Ser Gly Trp Thr Glu Glu Asp Gly Pro Lys Glu Gly Leu Ala			
	595	600	605
Glu Tyr Ile Val Glu Phe Leu Lys Lys Lys Ala Glu Met Leu Ala Asp			
	610	615	620
Tyr Phe Ser Leu Glu Ile Asp Glu Glu Gly Asn Leu Ile Gly Leu Pro			
	625	630	635
			640



Leu Leu Ile Asp Asn Tyr Val Pro Pro Leu Glu Gly Leu Pro Ile Phe  
                     645                                    650                                    655  
 Ile Leu Arg Leu Ala Thr Glu Val Asn Trp Asp Glu Glu Lys Glu Cys  
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 Phe Glu Ser Leu Ser Lys Glu Cys Ala Met Phe Tyr Ser Ile Arg Lys  
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 Gln Tyr Ile Ser Glu Glu Ser Thr Leu Ser Gly Gln Gln Ser Glu Val  
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 Pro Gly Ser Ile Pro Asn Ser Trp Lys Trp Thr Val Glu His Ile Val  
                     705                                    710                                    715                                    720  
 Tyr Lys Ala Leu Arg Ser His Ile Leu Pro Pro Lys His Phe Thr Glu  
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<212> DNA

<213> Homo sapiens

<400> 14

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<212> PRT

<213> Homo sapiens

<400> 15

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 35 40 45

Ala Gly Ala Thr Asn Ile Asp Leu Lys Leu Lys Asp Tyr Gly Val Asp  
 50 55 60

Leu Ile Glu Val Ser Asp Asn Gly Cys Gly Val Glu Glu Glu Asn Phe  
 65 70 75 80

Glu Gly Leu Thr Leu Lys His His Thr Ser Lys Ile Gln Glu Phe Ala  
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 Asp Leu Thr Gln Val Glu Thr Phe Gly Phe Arg Gly Glu Ala Leu Ser  
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